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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/619,032	MURPHY ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *33* is/are allowed.

6)☒ Claim(s) *1-3,5-13,15,17-32* is/are rejected.

7)☒ Claim(s) *4,14,16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 1-33 are pending.

Applicant's amendment of claims 1-2, 17-27, addition of claims 28-33 in a communication filed on 6/4/2004 is acknowledged.

Applicant's submission of a declaration by inventor Jay Short under 37 CFR 1.132 in a communication filed on 6/14/2004 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

1. Claims 22-24 are objected to due to the recitation of "polypeptide comprises at least x% amino acid sequence identity". For clarity and consistency, it is suggested that the term be amended to recite "polypeptide has at least X% amino acid sequence identity". It is noted that this language was used in claim 21, from which the instant claims depend. Appropriate correction is required.

2. Claim 28 is objected to due to the recitation of "compound having the ...bond comprises a saccharide and polypeptide is contacted...". For clarity and consistency, it is suggested that the term be amended to recite "compound having the ...bond comprises a saccharide and the polypeptide is contacted...". Appropriate correction is required.

3. Claim 29 is objected to due to the recitation of "saccharide comprises a polysaccharide or an oligosaccharide". For clarity, it is suggested that the term be amended to recite "saccharide is a polysaccharide or an oligosaccharide" since the term "comprise" can be understood to mean "have". Appropriate correction is required.

4. Claim 31 is objected to due to the recitation of "oligosaccharide comprises a raffinose, a stachyose...". ". For clarity, it is suggested that the term be amended to recite "oligosaccharide is a raffinose, a stachyose..." since the term "comprise" can be understood to mean "have". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 30 is indefinite in the recitation of "polysaccharide or oligosaccharide further comprises a legume" as it is unclear how a sugar molecule can comprise a legume, which is a vegetable. For examination purposes, it will be assumed that the term reads "polysaccharide or oligosaccharide is found in a legume". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 3, 15, 18-24, 26-27 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

10. Applicants argue that the claimed invention is sufficiently described so that one of skill in the art would recognize that Applicants were in possession of the claimed invention at the time of filing. According to Applicants, the genus of products required to practice the claimed method has been described in terms of physico-chemical properties and function. Applicants refer to Example 14 of the USPTO Written Description Guidelines as shown in Exhibit A and assert that procedures for making the variants in that example are known in the art . Therefore, it is Applicant's contention that the claimed invention meets the written description requirements for the same reasons indicated in Example 14 of the guidelines. Applicants further submit that the claims fully comply with the written description requirements as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) and conclude that those of skill in the art would recognize Applicant's possession of the claimed invention, citing *Vas-cath Inc. V. Mahukar,* 19 USPQ2d 1 111, (Fed Cir. 1991). Applicants also submit that the specification does not have to describe structural features required for the genus of polypeptides to have the desired activity and assert that in Example 14, it was found that the genus claimed met the written description requirement without setting forth any specific structural features. Applicants refer to a declaration by inventor Jay Short and state that in such declaration, Dr. Short indicates that procedures for identifying α-galactosidase fragments and variants are conventional and routine in the art.

11. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 3, 15, 18-24, 26-27. The Examiner acknowledges Dr Short's declaration and agrees that the claims recite structural and functional limitations in regard to the genus of products required to practice the claimed invention. However the Examiner disagrees with Applicant's contention that the instant case is analogous to Example 14 of the guidelines or that the claims fully comply with the written description requirements as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997).

As repeatedly indicated in previous Office Actions, a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by an amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. While 95% sequence identity can be considered to be a substantial portion of the genus since only 5% of the structure is variable, as indicated in Example 14, the instant claims do not recite a representative number of species nor do they recite structural features which one of skill in the art would consider a substantial portion of the genus. Claims 3, 15, 20-24, 26-27 are directed to a method which requires a genus of polypeptides having α-galactosidase activity wherein said polypeptides comprise fragments ranging from 30-50 consecutive amino acids of SEQ ID NO: 4 or 30-50 amino acids of a polypeptide having at least 70%, 80%, 90% or 95% sequence identity to SEQ ID NO: 4. Therefore, at best, the structural elements recited constitute between 8% up to 14% of the total structure of the polypeptide of SEQ ID NO: 4 (364 amino acids; 8%=30x100/364; 14%=50x100/364).). In the case of claims 20-24 and 26-27, the structural elements shared constitute less than the range indicated above (8%-14% of the structure of SEQ ID NO: 4) in view of the fact that these structural elements are derived from a polypeptide having at least 70% sequence identity to SEQ ID NO: 4. Claims 18-19, 26, 27 are directed to a method which requires a genus of polypeptides having α-galactosidase activity wherein said polypeptides result from conservatively substituting any number of amino acids in the polypeptide of SEQ ID NO: 4. Thus, the structural limitation recited in said claims, i.e. any number of conservative substitutions in the polypeptide of SEQ ID NO: 4, is not deemed to encompass a substantial portion of the genus in view of the fact that this genus encompass species which would have little or no structural elements in common with the polypeptide of SEQ ID NO: 4. Any amino acid in the polypeptide of SEQ ID NO: 4 can be conservatively substituted for another amino acid. In view of the structural elements recited in the claims, one of skill in the art cannot reasonably

conclude that the claimed genus complies with the written description requirements as set forth in *University of California v. Eli Lilly & Co.*, or that the instant case is analogous to that in Example 14 of the guidelines.

Furthermore, while it is agreed that the art teaches methods to create variants as those recited in the claims and assays to detect α-galactosidase activity are known, it is noted that in the written description analysis, the issue being discussed is whether one of skill in the art would recognize that the disclosure of one single species, i.e. the polypeptide of SEQ ID NO: 4, is sufficient to describe a large structurally variable genus as that recited in the claims. As indicated in previous Office Actions, the art teaches that even polypeptides sharing a high level of structural similarity do not share the same function. Therefore, it is clear from the references previously cited that, absent some knowledge or guidance as to how structure correlates with function, a single polypeptide disclosed is not sufficient to describe structurally similar polypeptides having the same function. As indicated in the guidelines, a representative number of species is required to adequately describe the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. Therefore, in the instant case, the disclosure of a single species is not deemed sufficient to adequately describe the genus of products required to practice the claimed invention.

12. Claims 1-3, 5-13, 15, 17-27 remain rejected and newly added claims 28-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for hydrolyzing α-glycosidic bonds with the polypeptide of SEQ ID NO: 4, does not reasonably provide enablement for a method for hydrolyzing hydrolyzing α-glycosidic bonds with a polypeptide having α-galactosidase activity wherein the polypeptide (1) has at least 70%

sequence identity to SEQ ID NO: 4, (2) is encoded by a nucleic acid which hybridizes at the conditions recited in the claims, (3) which results from any number of conservative substitutions in the polypeptide of SEQ ID NO: 4, or (4) which comprises fragments of the polypeptide of SEQ ID NO: 4 or fragments of a polypeptide having at least 70%, 80%, 90% or 95% sequence identity to SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

13. Applicants argue that the specification enabled the skilled artisan at the time of the invention to identify, make and use the genus of polypeptides used in the claimed invention. Applicants refer to a declaration by inventor Jay Short and indicate that in that declaration, Dr. Short states that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art was very high in regard to screening enzymes and nucleic acids encoding enzymes having α-galactosidase activity. Applicants submit that Dr. Short declares that the creation of variants would not have required any knowledge or guidance as to which specific structural elements correlate with α-galactosidase activity. Applicants further point out that Dr. Short declares that methods known at the time of the invention for modifying nucleic acids or proteins in combination with high throughput enzyme activity screening made knowledge of protein structure obsolete and unnecessary. Applicants submit that Dr. Short indicates that the specification presented to the skilled artisan a rational and a predictable scheme for modifying the polypeptide of SEQ ID NO: 4 with an expectation of obtaining the desired function.

14. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 1-3, 5-13, 15, 17-27 or to avoid the rejection of newly added claims 28-32. The Examiner acknowledges the declaration by Dr. Short and agrees that at the time of filing, methods to create the variants required to practice the claimed method were known in the art. However, the Examiner disagrees with Applicant's contention that the specification

enables the full scope of the claims or that practicing the claimed invention would not constitute undue experimentation. Claims 1-2, 5-13, 25, 28-32 are directed to a method which requires polypeptides having α-galactosidase activity which have at least 70%, 80% or 90% sequence identity to SEQ ID NO: 4. Claim 17 is directed to a method which requires polypeptides encoded by nucleic acids which hybridize to the polynucleotide of SEQ ID NO: 3 under conditions of low stringency. Claims 3, 15, 20-24, 26-27 are directed to a method which requires polypeptides having α-galactosidase activity wherein said polypeptides comprise fragments ranging from 30-50 consecutive amino acids of SEQ ID NO: 4 or 30-50 amino acids of a polypeptide having at least 70%, 80%, 90% or 95% sequence identity to SEQ ID NO: 4. Claims 18-19, 26, 27 are directed to a method which requires polypeptides having α-galactosidase activity wherein said polypeptides result from conservatively substituting any number of amino acids in the polypeptide of SEQ ID NO: 4.

The scope of the claims is not commensurate with the enablement provided in regard to the large number of proteins encompassed by the claims for which only a small fraction of the structure is known, as well as the lack of knowledge in regard to the structural elements required in the claimed polypeptides such that they display the desired activity. As repeatedly indicated in previous Office Actions, the specification while disclosing the structure of the polypeptide of SEQ ID NO: 4 and that of the corresponding polynucleotide, i.e. SEQ ID NO: 3, fails to disclose the structural elements in SEQ ID NO: 3 or 4 or fragments thereof which correlate with the desired activity. There is no clue as to which are the structural elements which can be conservatively substituted in the polypeptide of SEQ ID NO: 4 and still retain α-galactosidase activity or which structural elements can be modified in the polypeptide of SEQ ID NO: 4 to obtain a 70%, 80% or 90% structural homolog having the same activity as that of the polypeptide of SEQ ID NO: 4. Similarly, no teaching has been presented in regard to which are the structural elements of the polynucleotide of SEQ ID NO: 3 which should be present in a nucleic acid which

hybridizes under the low stringency conditions recited such that it encodes an α-galactosidase. It is noted that the conditions recited in claim 17 are deemed low stringency conditions in view of the low temperature used in the wash step, i.e. room temperature. As known in the art, in general high stringency conditions would include wash steps at temperatures higher than 65 C if no formamide is used. Therefore, in view of the low stringency conditions recited, the genus of nucleic acids required would encompass nucleic acids having low sequence identity to the polynucleotide of SEQ ID NO: 3. It is reiterated herein that the art as previously discussed teaches that even minor structural changes can result in major changes in function. See particularly the teachings of Broun et al., Seffernick et al. and Witkowski et al. previously presented where it is shown that even homologs sharing more than 95% sequence identity do not share the same function. Thus, in the absence of some teaching or suggestion as to how structure correlates with the desired function, one of skill in the art would have to go through the burden of undue experimentation to determine which structural homologs of the polypeptide of SEQ ID NO: 4 display α-galactosidase activity to enable the full scope of the invention.

While methods to create the variants required by the invention and assays to determine α-galactosidase activity are known in the art, it is noted that testing the extremely large number of variants encompassed by the claims when there is no guidance or knowledge as to which are the structural elements in the polypeptide of SEQ ID NO: 4 which correlate with the desired activity, i.e. α-galactosidase activity, would constitute undue experimentation in view of the fact that it is not routine in the art to create an infinite number of variants and test them for activity. Instead, one of skill in the art would require some knowledge or guidance as to how structure correlates with function such that a reasonable number of variants with the potentiality of having the desired function can be created and tested. Thus, in view of the information provided, the lack of relevant examples, the lack of knowledge as to which structural elements in the polypeptide of SEQ ID NO: 4 correlate with the desired function, and the unpredictability of the art regarding

functional annotation based solely on structural homology, one of skill in the art cannot reasonably conclude that the specification enables the full scope of the claimed invention.

Allowable Subject Matter

15. Claim 33 appears to be allowable over the prior art of record.

16. Claims 4, 14, 16 appear to be allowable over the prior art of record but are objected to since they depend upon a rejected base claim.

Conclusion

17. No claim is in condition for allowance.

18. Applicant's amendment of claims 1-2, 17-27 and/or addition of claims 28-33 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94

(December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
July 16, 2004

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